STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 104718

TO: Jeffrey Parkin
Location: CM1/8E15
Art Unit: 1648
Thursday, October 09, 2003
Case Serial Number: 09549186

From: Paul Schulwitz
Location: Biotech-Chem Library
CM1-6B06
Phone: 305-1954

paul.schulwitz@uspto.gov

Search Notes

Examiner Parkin,

See attached results.

If you have any questions about this search feel free to contact me at any time.

Thank you for using STIC search services!

Paul Schulwitz
Technical Information Specialist
STIC Biotech/Chem Library
(703)305-1954

STIC SEARCH RESULTS FEEDBACK FORM

Biotech-Chem Library

Questions about the scope or the results of the search? Contact ***the searcher or contact***:

Mary Hale, Information Branch Supervisor
308-4258, CM1-1E01

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 1610*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
  (journal articles, conference proceedings, new product announcements etc.)

- *Relevant prior art **not found**:*
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC/Biotech-Chem Library CM1 – Circ. Desk

Access DB# 104718
105698

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: JEFF PARKIN Examiner #: 72607 Date: 09/29/03
Art Unit: 1648 Phone Number 308-2227 Serial Number: 09/549,186
Mail Box and Bldg/Room Location CM01/8E15 Results Format Preferred (circle) PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____

_____

Earliest Priority Filing Date: _____

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search the attached, highlighted peptides to see if any IMMUNORETROIDS, RETRO-INVERSO, OR RETROPEPTIDES have been made from the sequences. (FP, FL, +SL peptides). There are modified D-peptides obtained from the ~~ff~~ FOOT-AND-MOUTH DISEASE VIRUS (FMDV).

9.55 - 9.59 (4)

1009 - 10.24 (15)

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STAFF USE ONLY

Searcher: _____

Searcher Phone #: _____

Type of Search

NA Sequence (#) _____

AA Sequence (#) 3

Vendors and cost where applicable

STN 158/158

Dialog _____

"optimum" conformation of a linear sequence, as well as to the rapid degradation of peptides injected into the animal. In the context of the invention, a study of the antigenic and immunogenic properties of retro-inverso (RI) analogues derived from the immunodominant loop of three variants of serotype A12 of FMDV was therefore undertaken. The sequences of these peptides and of the corresponding RI analogues are shown on Table 8 (note: the parent sequence of the peptide studied covers the region 141-159; a cysteine residue is added in the N-terminal position at the end of coupling).

TABLE 8

Sequences of synthetic peptides (region 141-159) derived from the immunodominant loop of three variants of serotype A12 of the virus of aphthous fever (FMDV).

FP peptide (strain USA) (SEQ ID NO:7) C-G^{141}-S-G-V-R-G-D-F-G-S-L-A-P-R-V-A-R-Q-L^{159}

FL peptide (SEQ ID NO:8) C-G^{141}-S-G-V-R-G-D-F-G-S-L-A-L-R-V-A-R-Q-L^{159}

SL peptide (strain A) (SEQ ID NO:9) C-G^{141}-S-G-V-R-G-D-S-G-S-L-A-L-R-V-A-R-Q-L^{159}

Sequences of the corresponding retro-inverso analogues

HO-m(R or S)Leu-q-r-a-v-r-(*)-a-l-s-G-(**)-d-G-r-v-G-s-G-c-NH_2

(**)	:	f	f	s
(*)	:	p	l	l

The study is divided into 3 parts:

1) Study of the antigenic properties of the analogues.

Sera of guinea-pigs immunized against the virus ("antivirion"), protein VP_1 ("anti-protein VP_1"), against peptide 141-159 (variant USA; "anti-FP peptide") and serum originating from guinea-pigs infected with the virus ("convalescent") are available. Normal serum (negative batch) of the guinea-pig serves as a control. The results are shown on Table 9. The two RIa and RIb

```
=> d que l4
L1             2 SEA FILE=REGISTRY ABB=ON  PLU=ON  CGSGVRGDFGSLAPRVARQL/SQSP
L2             0 SEA FILE=REGISTRY ABB=ON  PLU=ON  CGSGVRGDFGSLALRVARQL/SQSP
L3             0 SEA FILE=REGISTRY ABB=ON  PLU=ON  CGSGVRGDSGSLALRVARQL/SQSP
L4             3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 OR L2 OR L3
```

Sequence search on STN

=> d ibib abs ind hitstr l4 1-3

L4 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:489994 HCAPLUS
DOCUMENT NUMBER: 139:83614
TITLE: Intranasal immunization of guinea pigs with an immunodominant foot-and-mouth disease virus peptide conjugate induces mucosal and humoral antibodies and protection against challenge
AUTHOR(S): Fischer, D.; Rood, D.; Barrette, R. W.; Zuwallack, A.; Kramer, E.; Brown, F.; Silbart, L. K.
CORPORATE SOURCE: Center of Excellence for Vaccine Research, University of Connecticut, Storrs, CT, USA
SOURCE: Journal of Virology (2003), 77(13), 7486-7491
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Guinea pigs immunized intranasally with a keyhole limpet hemocyanin-linked peptide, corresponding to the prominent G-H loop of the VP1 protein of foot-and-mouth disease virus, raised substantial levels of antipeptide and virus-neutralizing antibodies in sera and of peptide-specific secretory IgA in nasal secretions. In groups of animals immunized intranasally without adjuvant, 86 percent were fully protected upon challenge with homotypic virus. Surprisingly, animals given the peptide conjugates plus the mucosal adjuvant cholera toxin were afforded only partial protection in that primary lesions were obsd. in most animals, although spread to other feet was prevented. These results indicate that intranasal inoculation with the peptide offers a potential route of vaccination against foot-and-mouth disease and may be useful for eliciting protection in the upper respiratory tracts of susceptible animals.
CC 15-2 (Immunochemistry)
ST foot mouth disease virus vaccination vaccine nose VP1
IT Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A, secretory; intranasal immunization of guinea pigs with an immunodominant foot-and-mouth disease virus peptide conjugate induces mucosal and humoral antibodies and immune protection)
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(VP1; intranasal immunization of guinea pigs with an immunodominant foot-and-mouth disease virus VP1 peptide conjugate induces mucosal and humoral antibodies and immune protection)
IT Immunostimulants
(adjuvants; intranasal immunization of guinea pigs with an immunodominant foot-and-mouth disease virus peptide conjugate induces mucosal and humoral antibodies and immune protection)
IT Toxins
RL: PAC (Pharmacological activity); BIOL (Biological study)
(cholera; intranasal immunization of guinea pigs with an immunodominant foot-and-mouth disease virus peptide conjugate induces mucosal and humoral antibodies and immune protection)
IT Disease, animal
(foot-and-mouth disease; intranasal immunization of guinea pigs with an immunodominant foot-and-mouth disease virus peptide conjugate induces mucosal and humoral antibodies and immune protection)

IT Foot-and-mouth disease virus
Immunity
Nose
Vaccines
(intranasal immunization of guinea pigs with an immunodominant foot-and-mouth disease virus peptide conjugate induces mucosal and humoral antibodies and immune protection)

IT Antibodies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(neutralizing; intranasal immunization of guinea pigs with an immunodominant foot-and-mouth disease virus peptide conjugate induces mucosal and humoral antibodies and immune protection)

IT Immunization
(vaccination, intranasal; intranasal immunization of guinea pigs with an immunodominant foot-and-mouth disease virus peptide conjugate induces mucosal and humoral antibodies and immune protection)

IT **199790-86-8D**, conjugates with carrier protein
RL: PAC (Pharmacological activity); BIOL (Biological study)
(intranasal immunization of guinea pigs with an immunodominant foot-and-mouth disease virus peptide conjugate induces mucosal and humoral antibodies and immune protection)

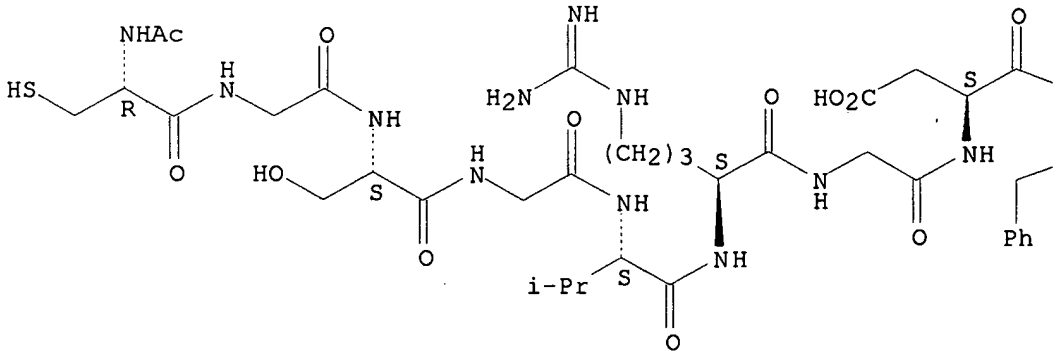
IT **199790-86-8D**, conjugates with carrier protein
RL: PAC (Pharmacological activity); BIOL (Biological study)
(intranasal immunization of guinea pigs with an immunodominant foot-and-mouth disease virus peptide conjugate induces mucosal and humoral antibodies and immune protection)

RN 199790-86-8 HCAPLUS

CN L-Leucine, N-acetyl-L-cysteinylglycyl-L-serylglycyl-L-valyl-L-arginylglycyl-L-.alpha.-aspartyl-L-phenylalanylglycyl-L-seryl-L-leucyl-L-alanyl-L-prolyl-L-arginyl-L-valyl-L-alanyl-L-arginyl-L-glutaminyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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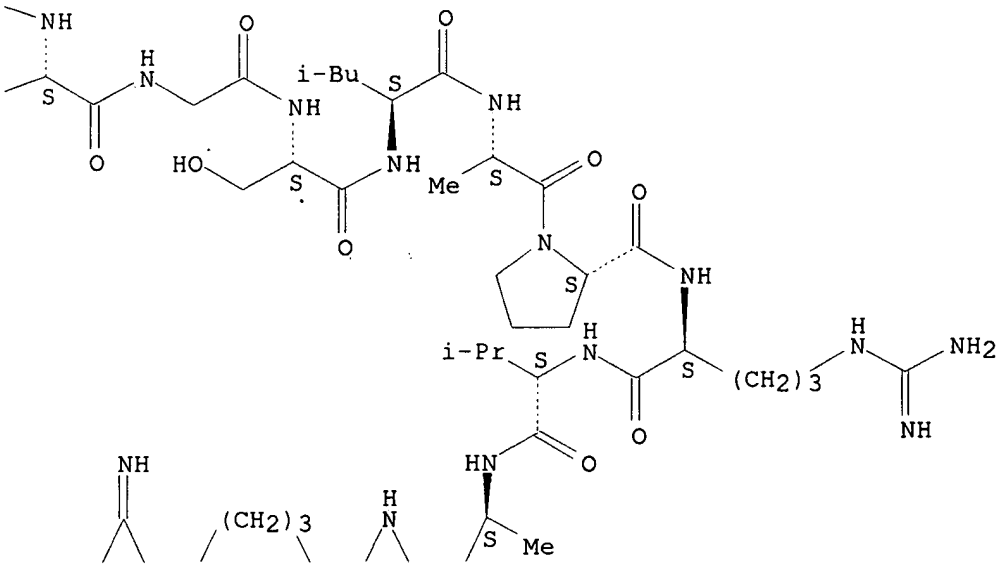

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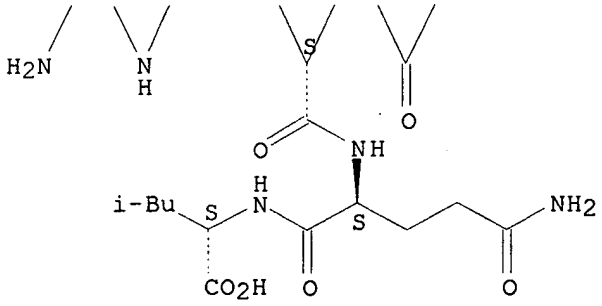


REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:597752 HCAPLUS
DOCUMENT NUMBER: 129:342490
TITLE: Mimicry of an immunodominant epitope of foot and mouth disease virus with retro-inverso isomers: a new approach in the design of peptide based vaccines
AUTHOR(S): Guichard, Gilles; Benkirane, Nadia; Briand, Jean-Paul; Muller, Sylviane; Van Regenmortel, Marc H. V.; Newman, John F. E.; Brown, Fred
CORPORATE SOURCE: Institut de Biologie Moleculaire et Cellulaire, UPR 9021 CNRS, Strasbourg, 67000, Fr.
SOURCE: Peptides 1996, Proceedings of the European Peptide

Symposium, 24th, Edinburgh, Sept. 8-13, 1996 (1998), Meeting Date 1996, 447-448. Editor(s): Ramage, Robert; Epton, Roger. Mayflower Scientific: Kingswinford, UK.
CODEN: 66RCA5
DOCUMENT TYPE: Conference
LANGUAGE: English

AB The retro-inverso analog of the immunodominant epitope 141-159 of the VP1 protein of foot-and-mouth disease virus was shown to induce in rabbits a peptide-specific neutralizing IgG response of much higher titer which lasted longer than that induced by the epitope.

CC 15-2 (Immunochemistry)

ST FMDV epitope retro inverso peptide neutralizing IgG

IT Immunoglobulins
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(G, neutralizing; mimicry of an immunodominant epitope of foot and mouth disease virus with retro-inverso isomers and induction of neutralizing antibodies)

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(VP1; mimicry of an immunodominant epitope of foot and mouth disease virus with retro-inverso isomers and induction of neutralizing antibodies)

IT Epitopes
Foot-and-mouth disease virus
(mimicry of an immunodominant epitope of foot and mouth disease virus with retro-inverso isomers and induction of neutralizing antibodies)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(retro-inverso; mimicry of an immunodominant epitope of foot and mouth disease virus with retro-inverso isomers and induction of neutralizing antibodies)

IT Vaccines
(synthetic; mimicry of an immunodominant epitope of foot and mouth disease virus with retro-inverso isomers and induction of neutralizing antibodies)

IT 199790-79-9 **199790-81-3 199790-86-8** 215603-35-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mimicry of an immunodominant epitope of foot and mouth disease virus with retro-inverso isomers and induction of neutralizing antibodies)

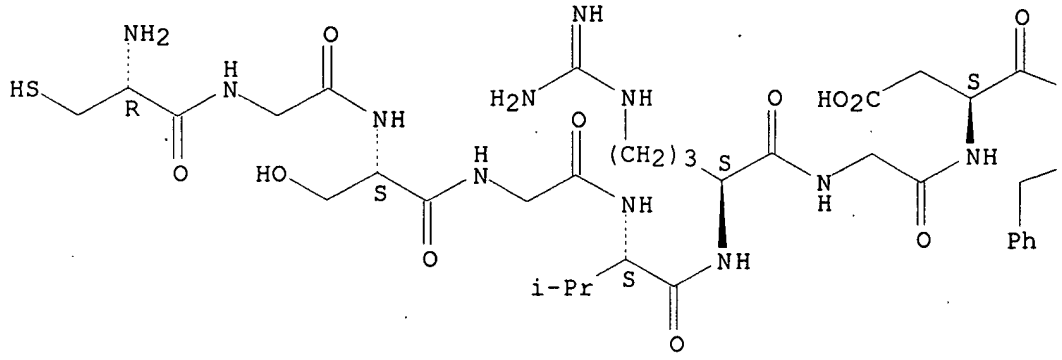
IT **199790-81-3 199790-86-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mimicry of an immunodominant epitope of foot and mouth disease virus with retro-inverso isomers and induction of neutralizing antibodies)

RN 199790-81-3 HCAPLUS

CN L-Leucine, L-cysteinylglycyl-L-serylglycyl-L-valyl-L-arginylglycyl-L-.alpha.-aspartyl-L-phenylalanylglycyl-L-seryl-L-leucyl-L-alanyl-L-prolyl-L-arginyl-L-valyl-L-alanyl-L-arginyl-L-glutaminyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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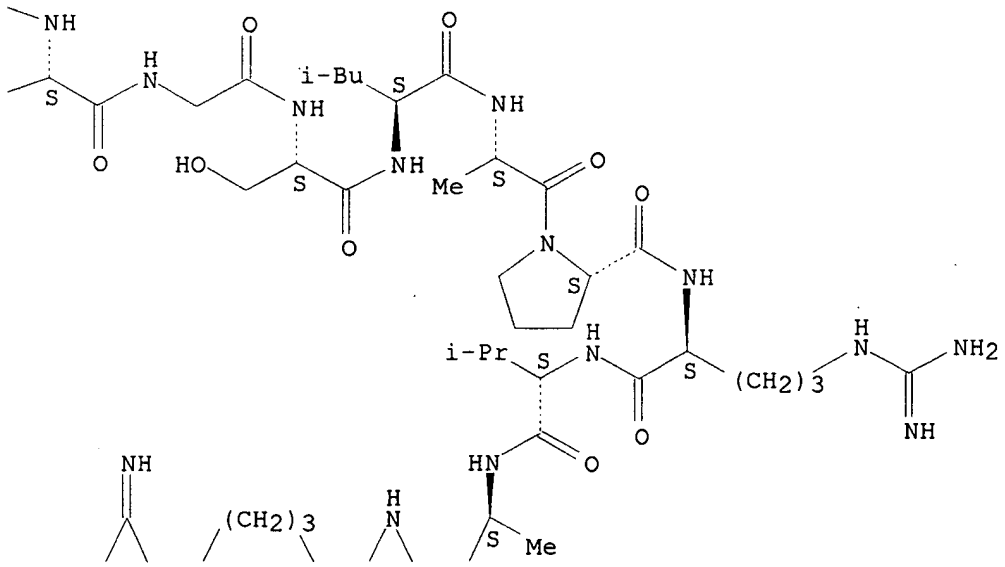

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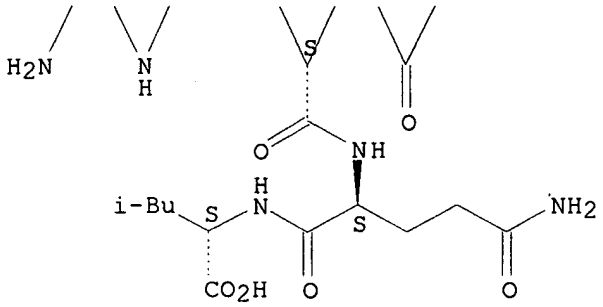
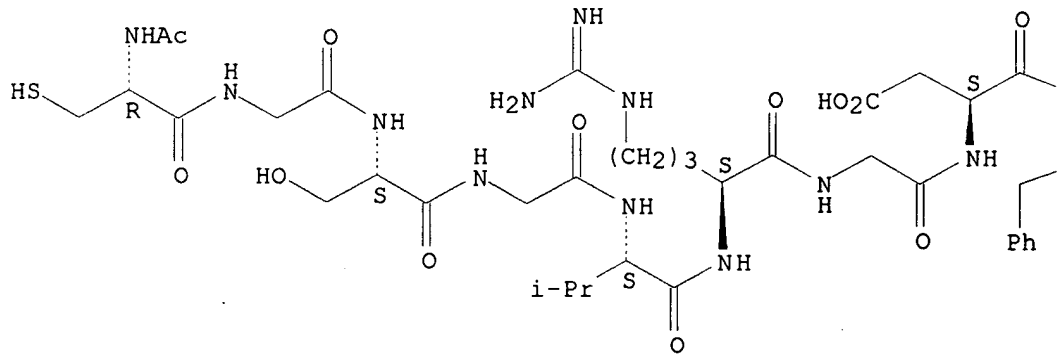


RN 199790-86-8 HCAPLUS
CN L-Leucine, N-acetyl-L-cysteinylglycyl-L-serylglycyl-L-valyl-L-arginylglycyl-L-.alpha.-aspartyl-L-phenylalanylglycyl-L-seryl-L-leucyl-L-alanyl-L-prolyl-L-arginyl-L-valyl-L-alanyl-L-arginyl-L-glutaminyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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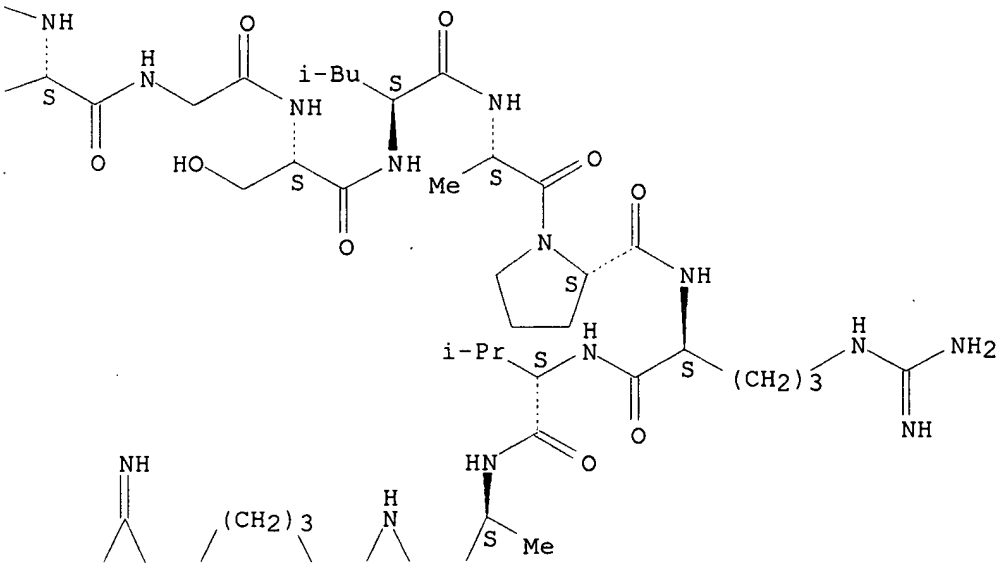
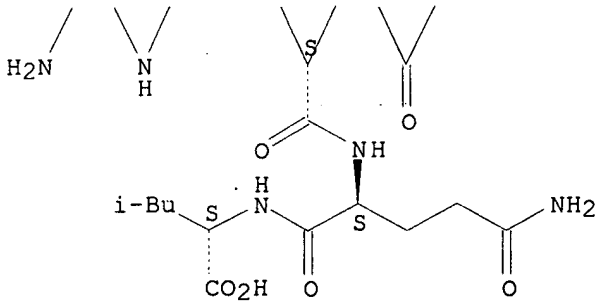


PAGE 2-B



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:768652 HCAPLUS
DOCUMENT NUMBER: 128:33517
TITLE: A retro-inverso peptide corresponding to the GH loop of foot-and-mouth disease virus elicits high levels of long-lasting protective neutralizing antibodies
AUTHOR(S): Briand, Jean-Paul; Benkirane, Nadia; Guichard, Gilles; Newman, John F. E.; Van Regenmortel, Marc H. V.; Brown, Fred; Muller, Sylviane
CORPORATE SOURCE: Unite Propre de Recherche 9021, Centre National de la Recherche Scientifique, Institut de Biologie Moleculaire et Cellulaire, Strasbourg, 67084, Fr.

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1997), 94(23), 12545-12550
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Peptides corresponding to the immunodominant loop located at residues 135-158 on capsid protein VP1 of foot-and-mouth disease virus (FMDV) generally elicit high levels of anti-peptide and virus-neutralizing antibodies. In some instances, however, the level of neutralizing antibodies is low or even negligible, even though the level of anti-peptide antibodies is high. The authors have shown previously that the antigenic activity of peptide 141-159 of VP1 of a variant of serotype A can be mimicked by a retro-inverso (all-D retro or retroenantio) peptide analog. This retro-inverso analog induced greater and longer-lasting antibody titers than did the corresponding L-peptide. The authors now show that a single inoculation of the retro-inverso analog elicits high levels of neutralizing antibodies that persist longer than those induced against the corresponding L-peptide and confer substantial protection in guinea pigs challenged with the cognate virus. In view of the high stability to proteases of retro-inverso peptide analogs and their enhanced immunogenicity, these results have practical relevance in designing potential peptide vaccines.

CC 15-2 (Immunochemistry)

ST retroinverso peptide foot mouth disease virus; neutralizing antibody vaccine foot mouth disease

IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(VP1; retro-inverso peptide corresponding to GH loop of foot-and-mouth disease virus elicitation of protective neutralizing antibodies in relation to vaccine)

IT Antibodies
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(neutralizing; retro-inverso peptide corresponding to GH loop of foot-and-mouth disease virus elicitation of protective neutralizing antibodies in relation to vaccine)

IT Foot-and-mouth disease virus
Peptidomimetics
Vaccines
(retro-inverso peptide corresponding to GH loop of foot-and-mouth disease virus elicitation of protective neutralizing antibodies in relation to vaccine)

IT Peptides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(retro-inverso; retro-inverso peptide corresponding to GH loop of foot-and-mouth disease virus elicitation of protective neutralizing antibodies in relation to vaccine)

IT 164259-71-6 199790-79-9 **199790-81-3** 199790-82-4
199790-83-5 199790-84-6 **199790-86-8** 199790-89-1
199790-90-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(retro-inverso peptide corresponding to GH loop of foot-and-mouth disease virus elicitation of protective neutralizing antibodies in relation to vaccine)

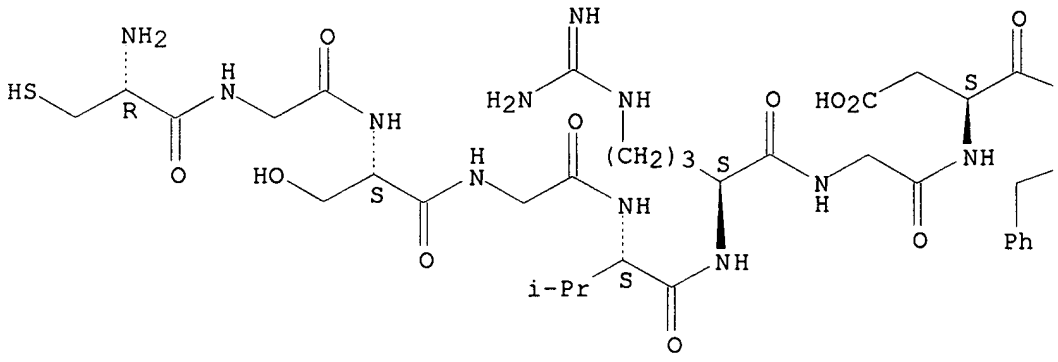
IT **199790-81-3 199790-86-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(retro-inverso peptide corresponding to GH loop of foot-and-mouth disease virus elicitation of protective neutralizing antibodies in relation to vaccine)

RN 199790-81-3 HCAPLUS

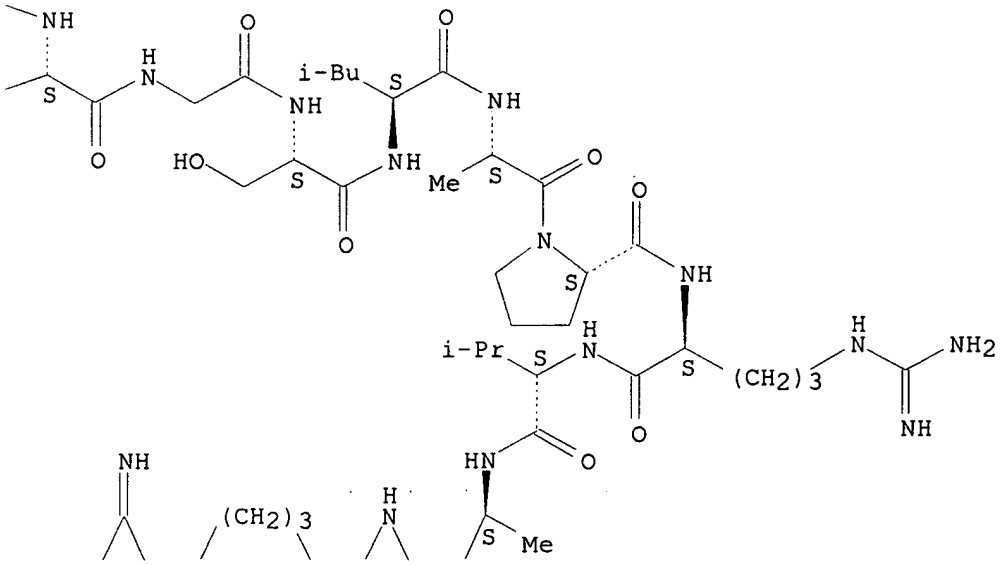
CN L-Leucine, L-cysteinylglycyl-L-serylglycyl-L-valyl-L-arginylglycyl-L-.alpha.-aspartyl-L-phenylalanylglycyl-L-seryl-L-leucyl-L-alanyl-L-prolyl-L-arginyl-L-valyl-L-alanyl-L-arginyl-L-glutaminyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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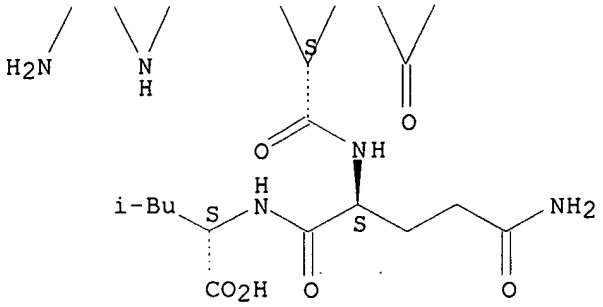
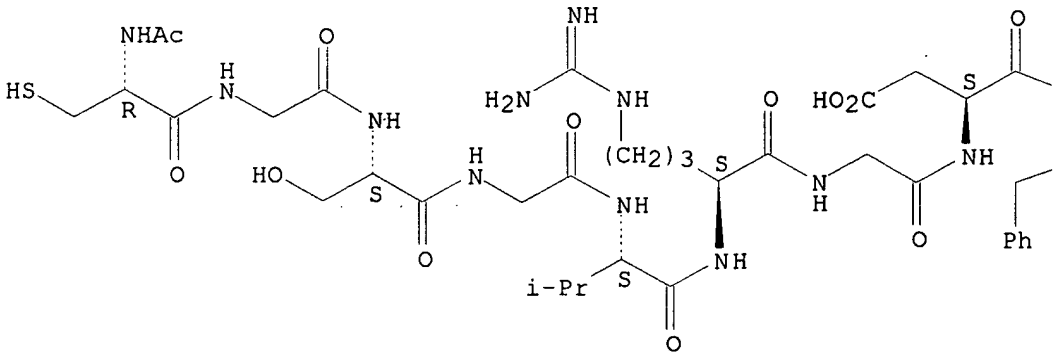


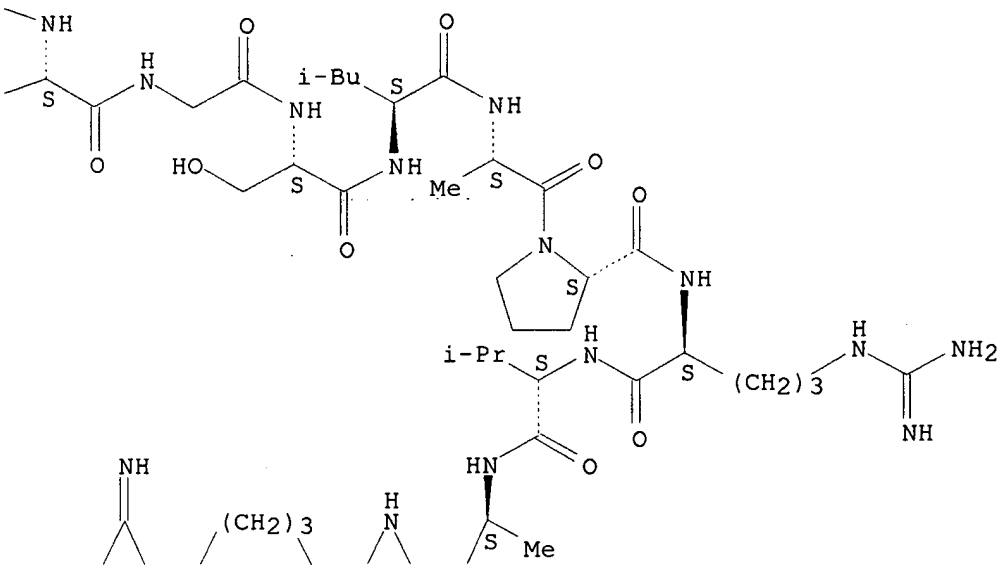
RN 199790-86-8 HCAPLUS
CN L-Leucine, N-acetyl-L-cysteinylglycyl-L-serylglycyl-L-valyl-L-arginylglycyl-L-.alpha.-aspartyl-L-phenylalanylglycyl-L-seryl-L-leucyl-L-alanyl-L-prolyl-L-arginyl-L-valyl-L-alanyl-L-arginyl-L-glutaminyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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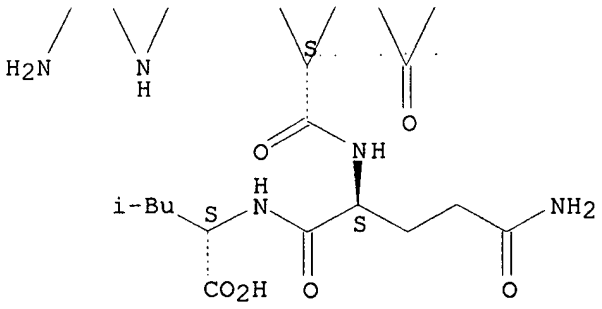

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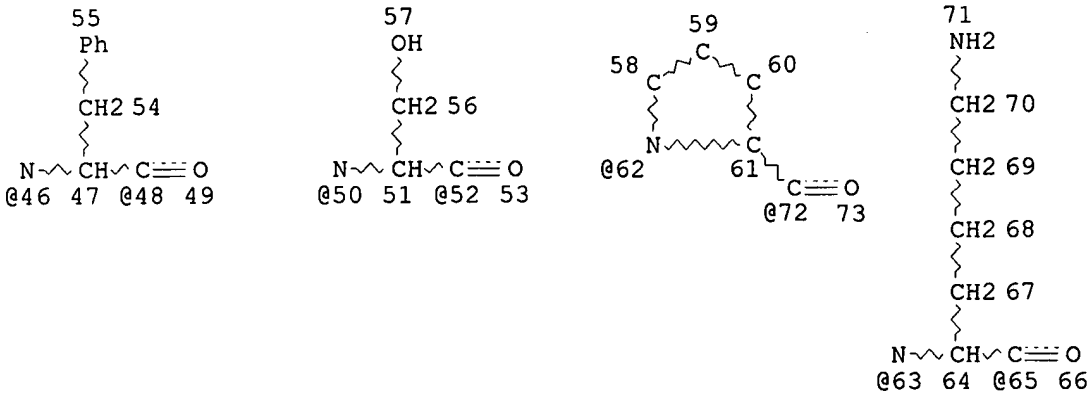

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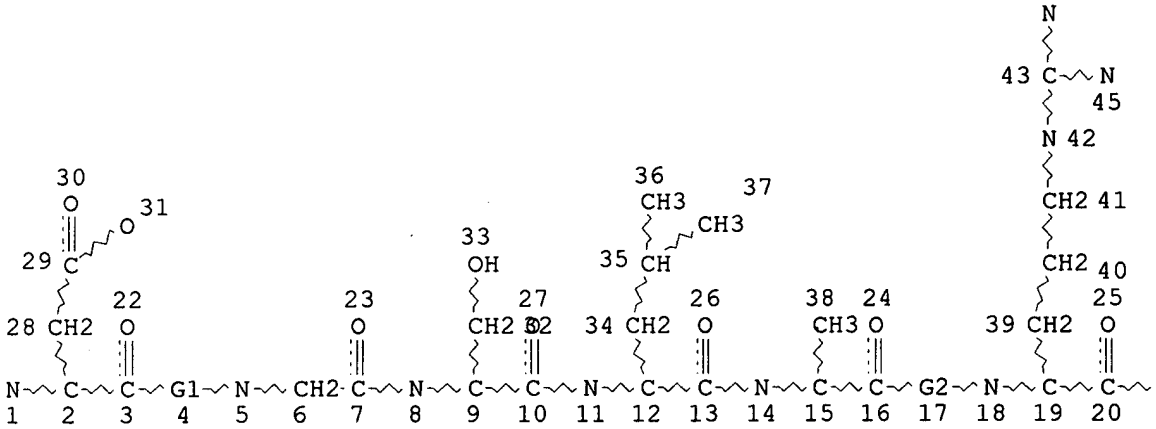

Page 2-A

Page 2-B
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CONNECT IS E3  RC AT   2
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CONNECT IS E3  RC AT  15
CONNECT IS E2  RC AT  18
CONNECT IS E3  RC AT  19
CONNECT IS E2  RC AT  21
CONNECT IS E1  RC AT  31
CONNECT IS E2  RC AT  42
CONNECT IS E3  RC AT  43
CONNECT IS E1  RC AT  44
CONNECT IS E1  RC AT  45
CONNECT IS E2  RC AT  58
CONNECT IS E2  RC AT  59
CONNECT IS E2  RC AT  60
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  73

STEREO ATTRIBUTES: NONE
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L8            26 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7
L11            6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8 AND FOOT? AND (IMMUNORET?
                 OR RETR?)
```

Structurally searched sequence for:

or open-D-(F/S)-G-S-L-A-(P/L)-R-open

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=> d ibib abs hitstr l11 1-6

L11  ANSWER 1 OF 6  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         1998:597752  HCAPLUS
DOCUMENT NUMBER:          129:342490
TITLE:                    Mimicry of an immunodominant epitope of foot
                          and mouth disease virus with retro-inverso
                          isomers: a new approach in the design of peptide based
                          vaccines
AUTHOR(S):                Guichard, Gilles; Benkirane, Nadia; Briand, Jean-Paul;
                          Muller, Sylviane; Van Regenmortel, Marc H. V.; Newman,
                          John F. E.; Brown, Fred
CORPORATE SOURCE:         Institut de Biologie Moleculaire et Cellulaire, UPR
                          9021 CNRS, Strasbourg, 67000, Fr.
SOURCE:                   Peptides 1996, Proceedings of the European Peptide
                          Symposium, 24th, Edinburgh, Sept. 8-13, 1996 (1998),
                          Meeting Date 1996, 447-448.  Editor(s): Ramage,
                          Robert; Epton, Roger.  Mayflower Scientific:
                          Kingswinford, UK.
                          CODEN: 66RCA5
DOCUMENT TYPE:            Conference
LANGUAGE:                 English
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AB The **retro**-inverso analog of the immunodominant epitope 141-159 of the VP1 protein of **foot**-and-mouth disease virus was shown to induce in rabbits a peptide-specific neutralizing IgG response of much higher titer which lasted longer than that induced by the epitope.

IT **199790-79-9 199790-81-3 199790-86-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mimicry of an immunodominant epitope of **foot** and mouth disease virus with **retro**-inverso isomers and induction of neutralizing antibodies)

RN 199790-79-9 HCAPLUS

CN L-Cysteine, glycyl-L-serylglycyl-L-valyl-L-arginylglycyl-L-.alpha.-aspartyl-L-phenylalanylglycyl-L-seryl-L-leucyl-L-alanyl-L-prolyl-L-arginyl-L-valyl-L-alanyl-L-arginyl-L-glutaminyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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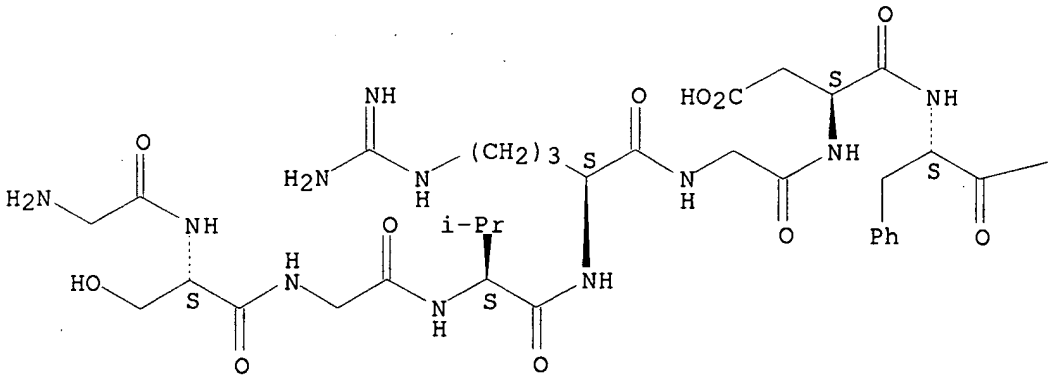

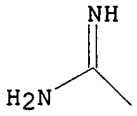

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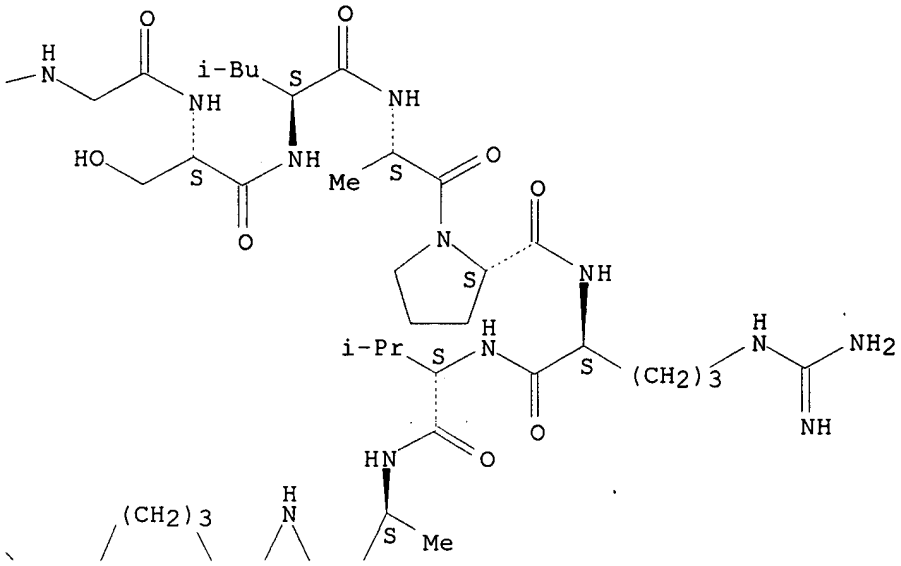

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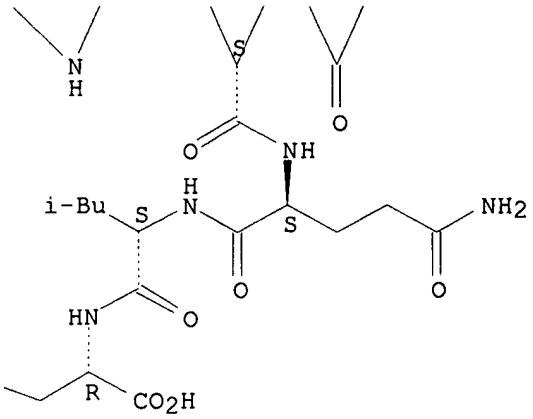

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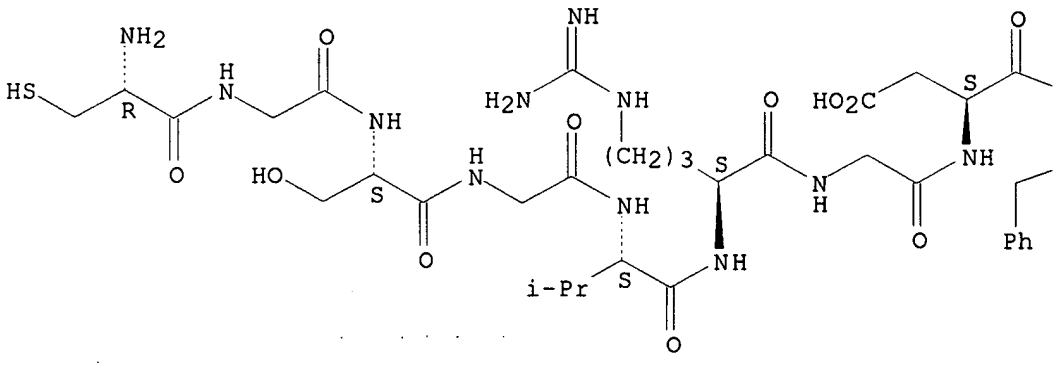
Absolute stereochemistry.

PAGE 1-A



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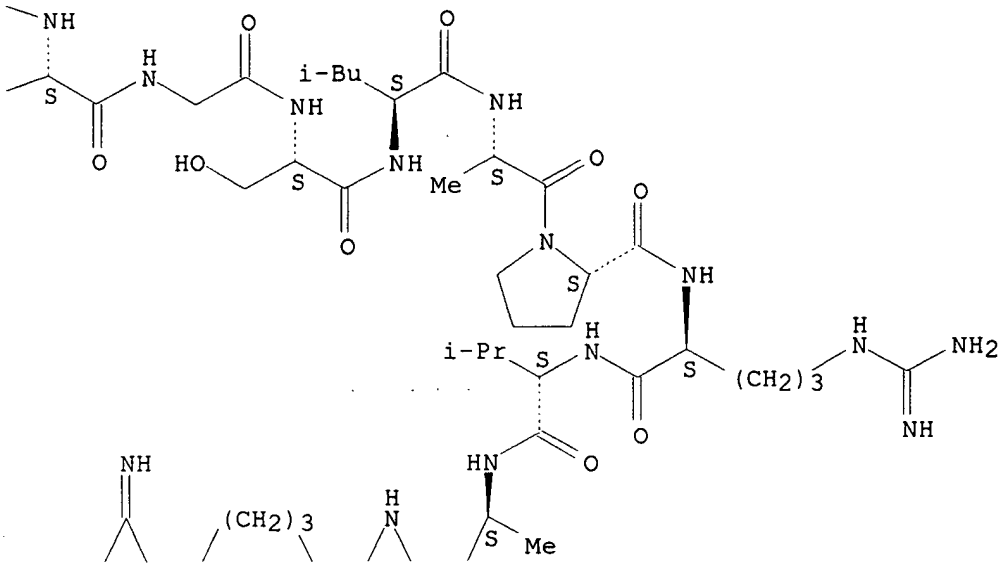

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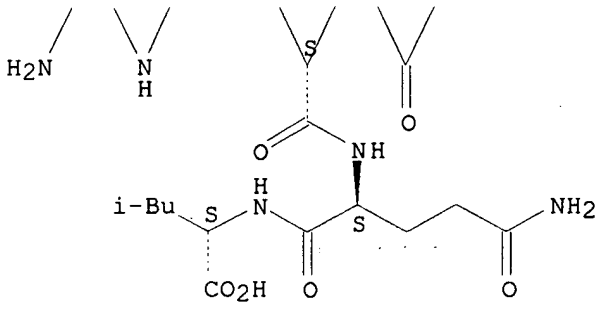

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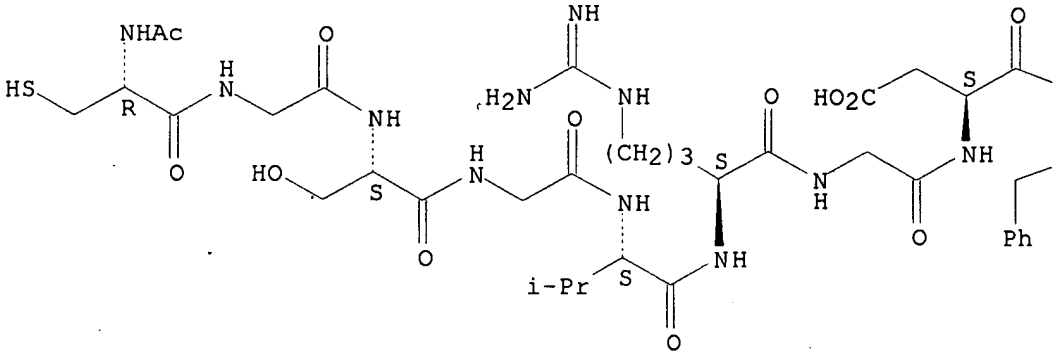
Absolute stereochemistry.

PAGE 1-A



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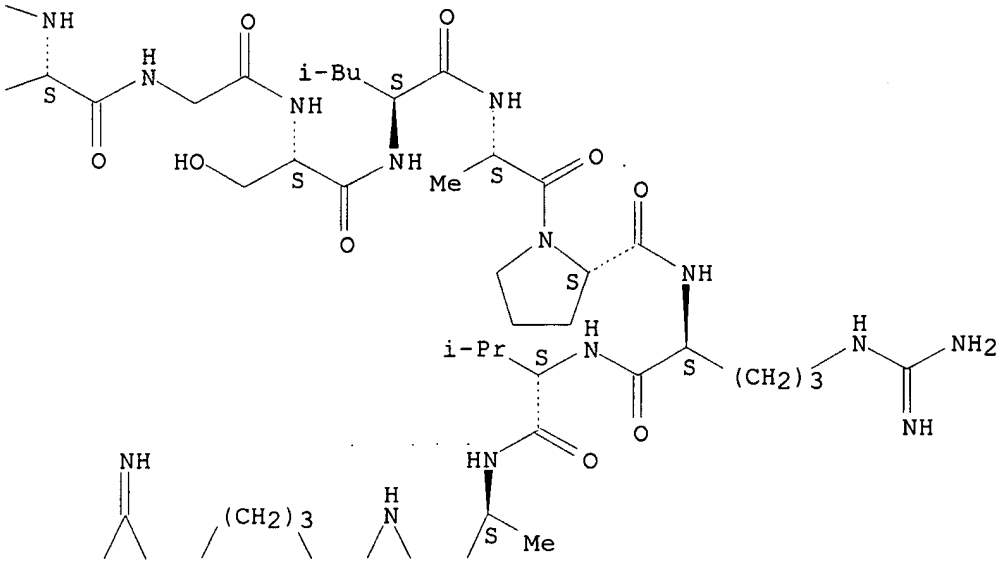

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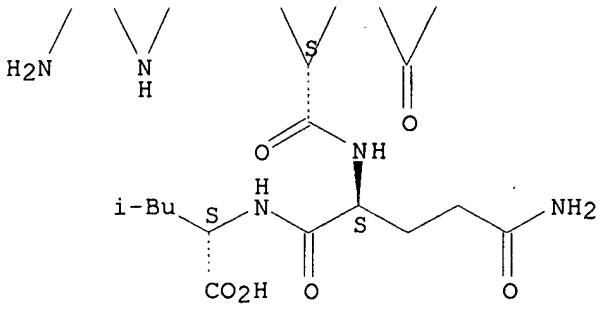

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:768652 HCAPLUS
DOCUMENT NUMBER: 128:33517
TITLE: A **retro**-inverso peptide corresponding to the GH loop of **foot**-and-mouth disease virus elicits high levels of long-lasting protective neutralizing antibodies
AUTHOR(S): Briand, Jean-Paul; Benkirane, Nadia; Guichard, Gilles; Newman, John F. E.; Van Regenmortel, Marc H. V.; Brown, Fred; Muller, Sylviane
CORPORATE SOURCE: Unite Propre de Recherche 9021, Centre National de la Recherche Scientifique, Institut de Biologie Moleculaire et Cellulaire, Strasbourg, 67084, Fr.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1997), 94(23), 12545-12550
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Peptides corresponding to the immunodominant loop located at residues 135-158 on capsid protein VP1 of **foot**-and-mouth disease virus (FMDV) generally elicit high levels of anti-peptide and virus-neutralizing antibodies. In some instances, however, the level of neutralizing antibodies is low or even negligible, even though the level of anti-peptide antibodies is high. The authors have shown previously that the antigenic activity of peptide 141-159 of VP1 of a variant of serotype A can be mimicked by a **retro**-inverso (all-D **retro** or **retroenantio**) peptide analog. This **retro**-inverso analog induced greater and longer-lasting antibody titers than did the corresponding L-peptide. The authors now show that a single inoculation of the **retro**-inverso analog elicits high levels of neutralizing antibodies that persist longer than those induced against the corresponding L-peptide and confer substantial protection in guinea pigs challenged with the cognate virus. In view of the high stability to proteases of **retro**-inverso peptide analogs and their enhanced immunogenicity, these results have practical relevance in designing potential peptide vaccines.

IT **164259-71-6 199790-79-9 199790-81-3 199790-82-4 199790-83-5 199790-86-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); PRP (Properties); BIOL (Biological study)
(**retro**-inverso peptide corresponding to GH loop of **foot**-and-mouth disease virus elicitation of protective neutralizing antibodies in relation to vaccine)

RN 164259-71-6 HCAPLUS

CN L-Leucine, glycyl-L-serylglycyl-L-valyl-L-arginylglycyl-L-.alpha.-aspartyl-L-phenylalanylglycyl-L-seryl-L-leucyl-L-alanyl-L-prolyl-L-arginyl-L-valyl-L-alanyl-L-arginyl-L-glutaminyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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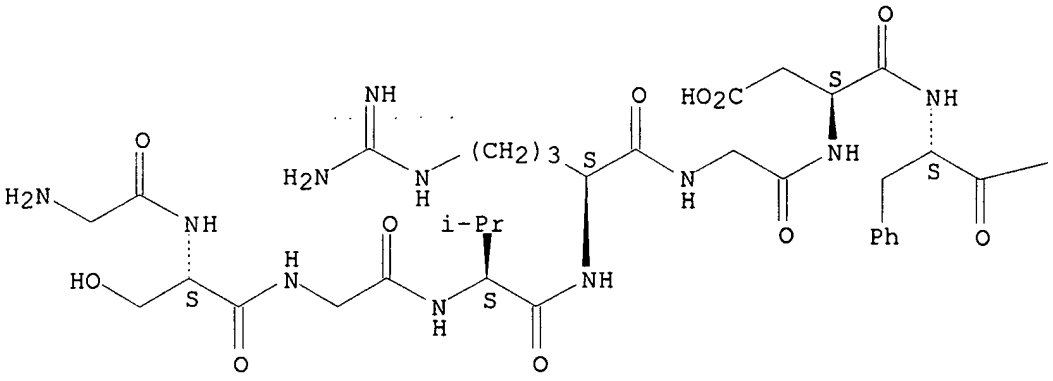

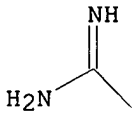

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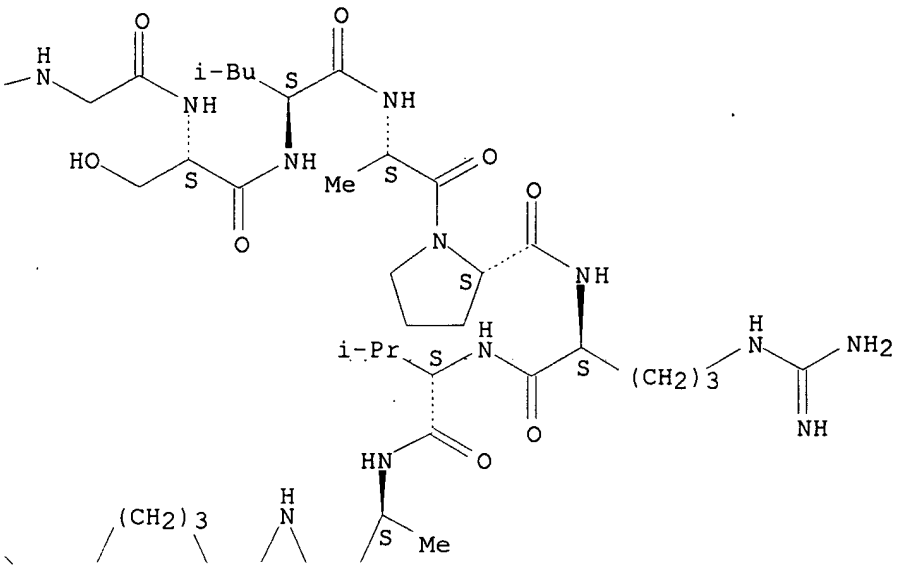

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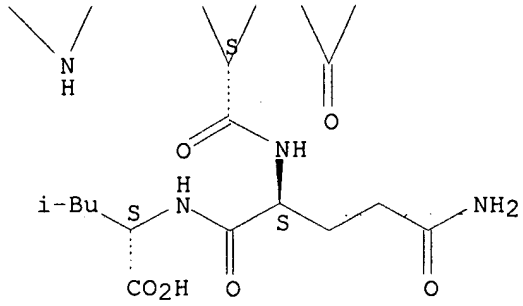

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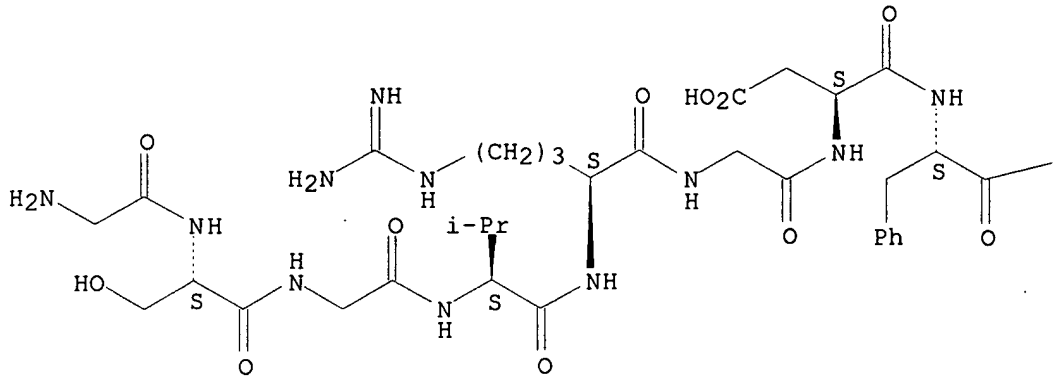
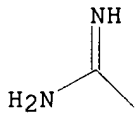
Absolute stereochemistry.

PAGE 1-A





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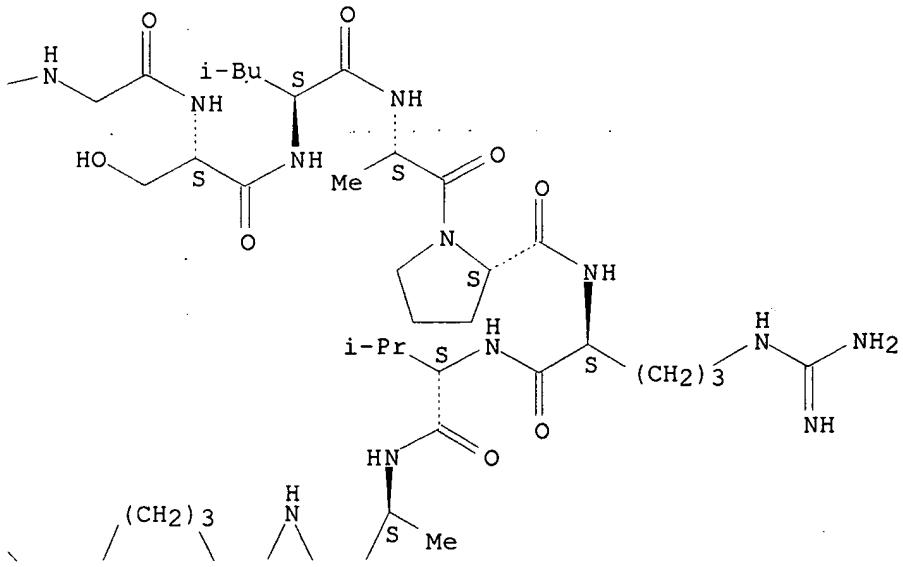

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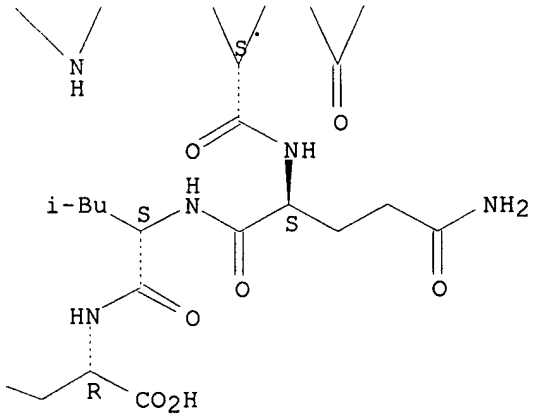
PAGE 2-B



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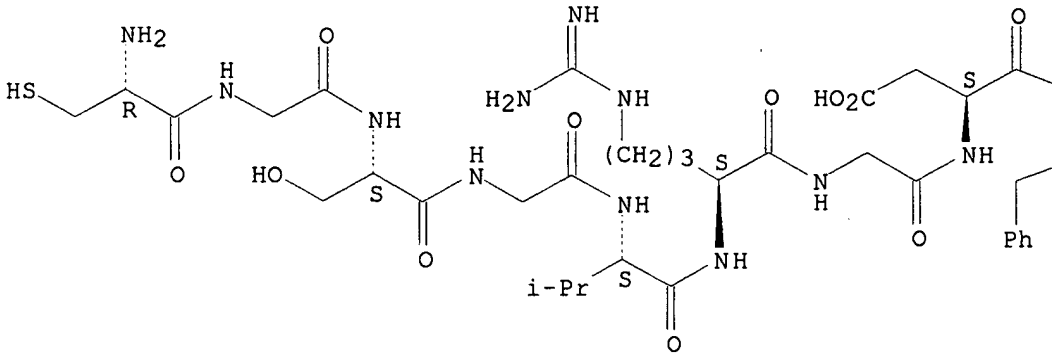
Absolute stereochemistry.

PAGE 1-A



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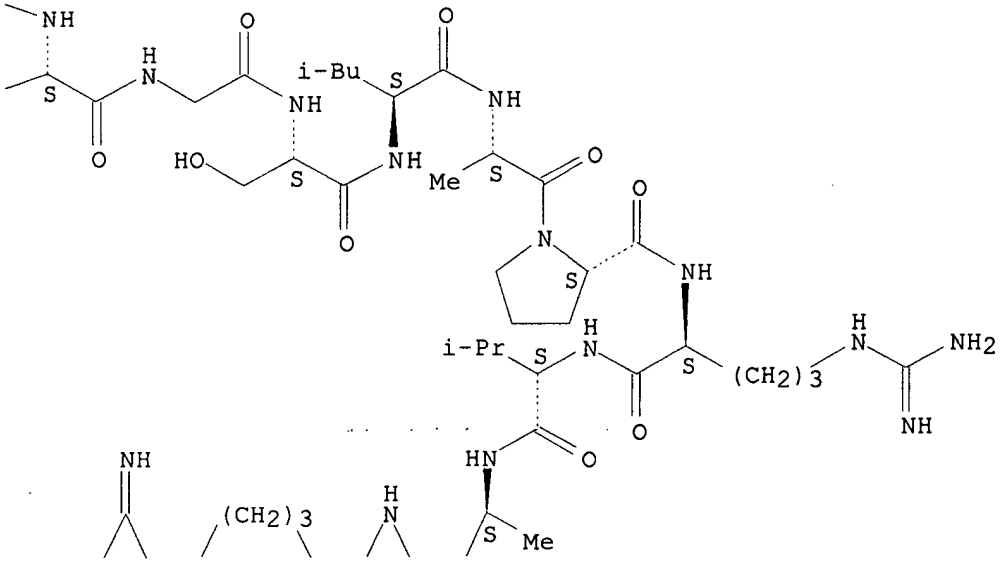

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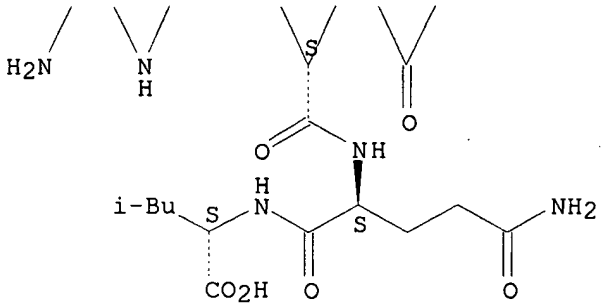

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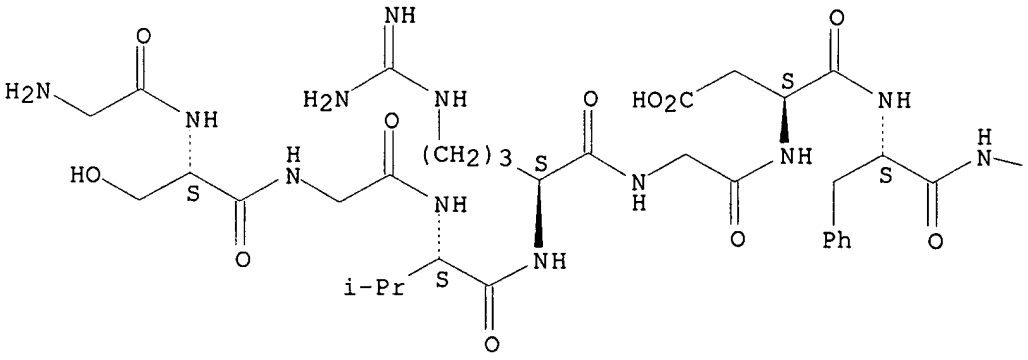
Absolute stereochemistry.

PAGE 1-A



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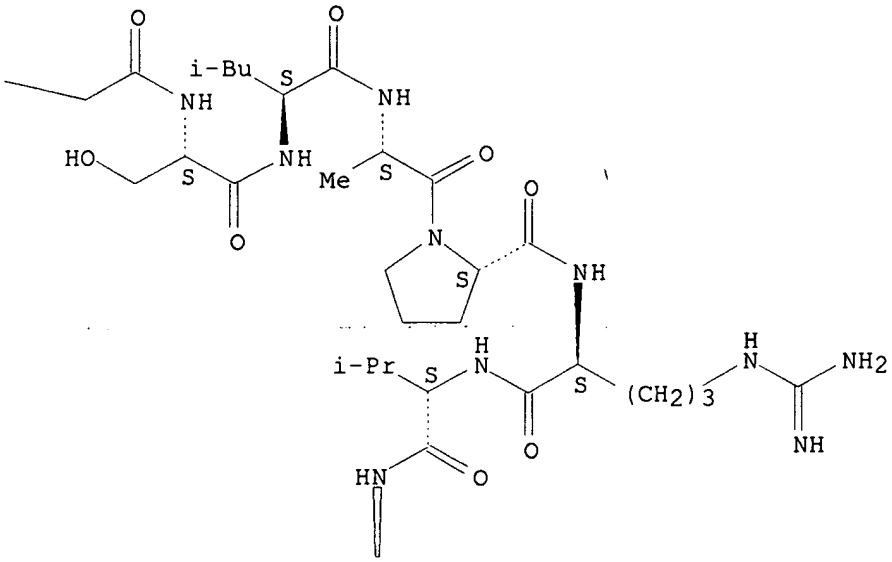

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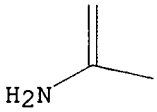

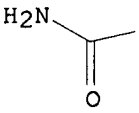

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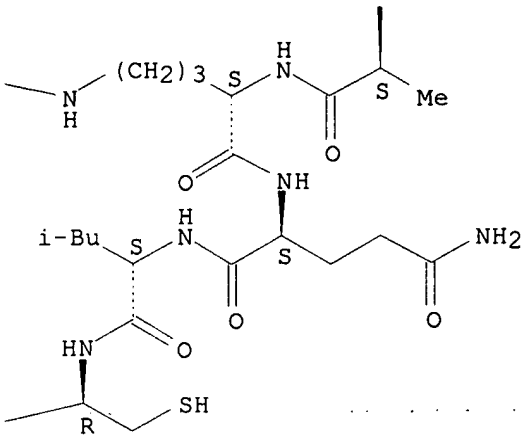

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Absolute stereochemistry.

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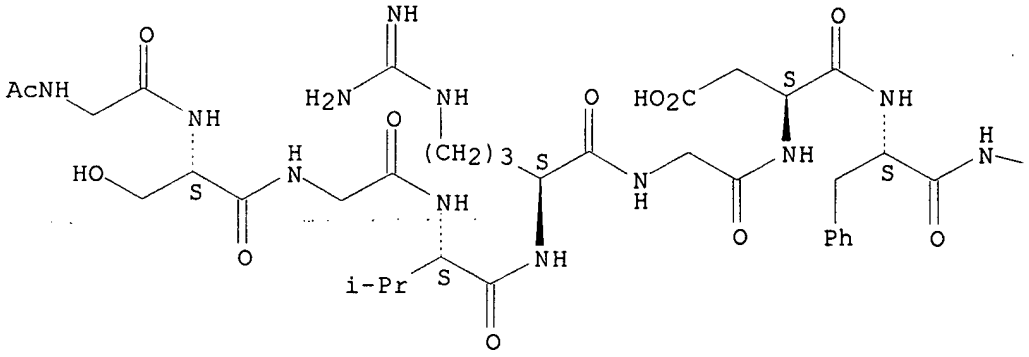

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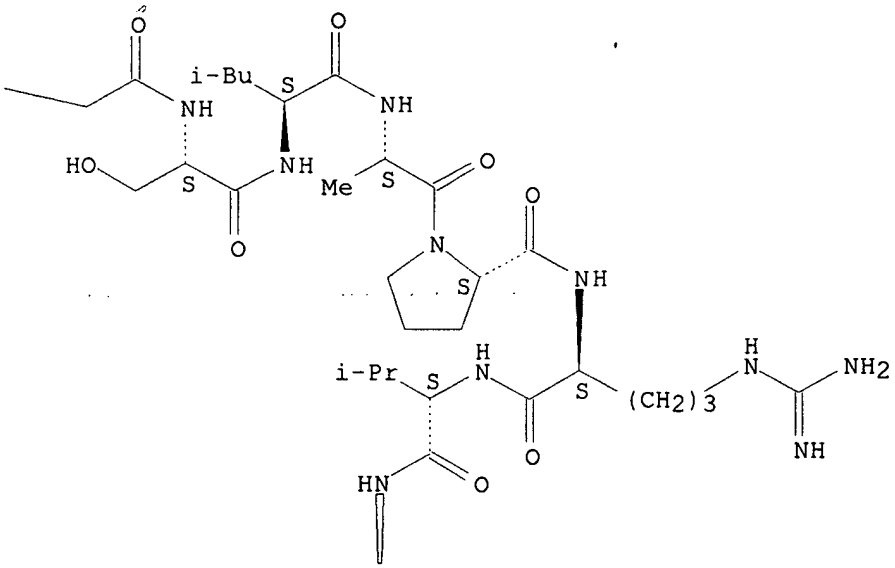

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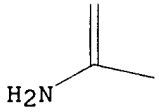

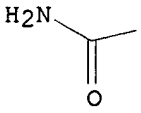

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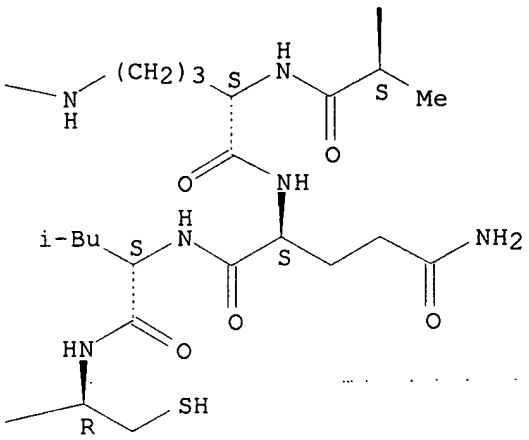

RN 199790-86-8 HCAPLUS
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Absolute stereochemistry.

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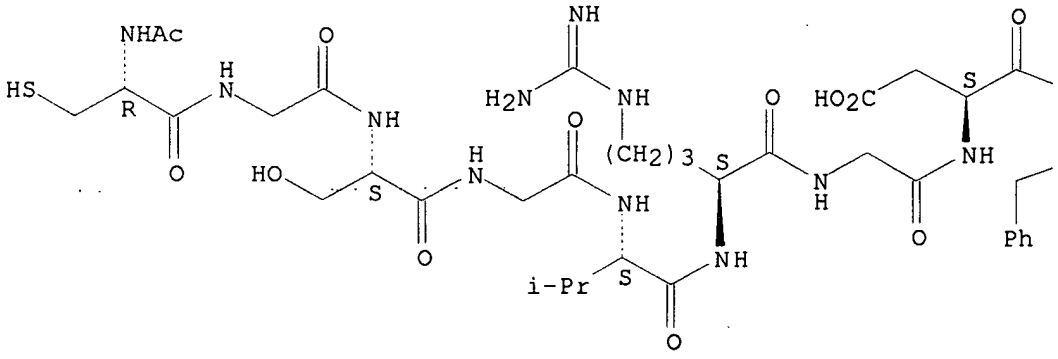

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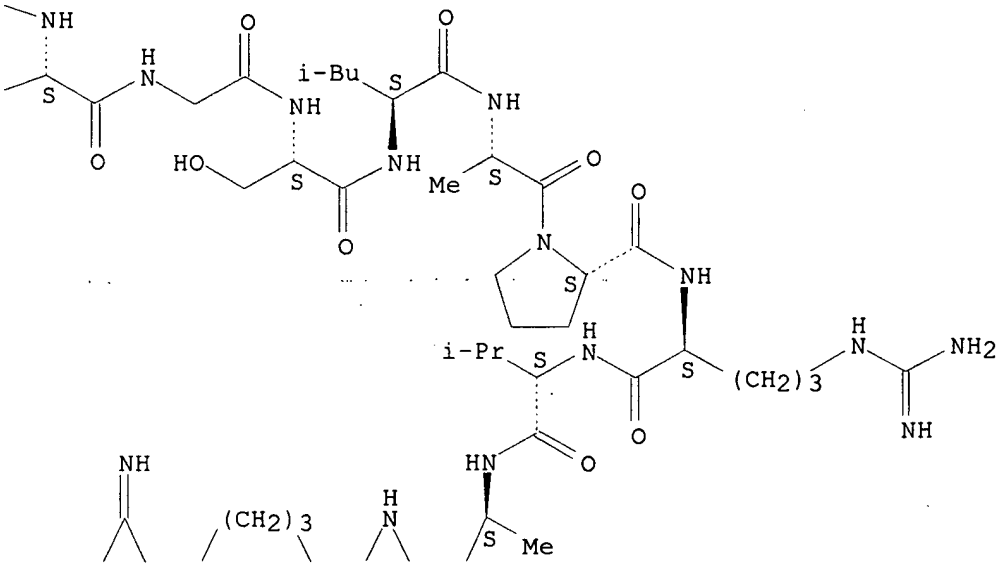

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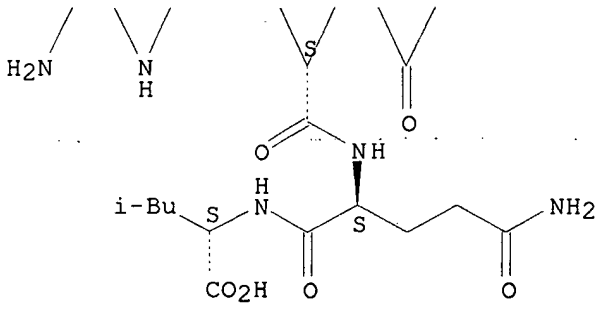

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L11 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:431945 HCAPLUS
DOCUMENT NUMBER: 127:175078
TITLE: Antigenic mimicry with an all-D-**retro** peptide corresponding to the immunodominant loop of **foot**-and-mouth disease virus
AUTHOR(S): Muller, Sylviane; Briand, Jean-Paul; Benkirane, Nadia; Guichard, Gilles; Van Regenmortel, Marc H.V.; Newman, John F.E.; Brown, Fred
CORPORATE SOURCE: Institut de Biologie Moleculaire et Cellulaire, UPR 9021, CNRS, Strasbourg, 67084, Fr.
SOURCE: Vaccines 97: Molecular Approaches to the Control of

Infectious Diseases, [Annual Meeting on Modern Approaches to the Control of Infectious Diseases], 14th, Cold Spring Harbor, N. Y., Sept. 9-13, 1996 (1997), Meeting Date 1996, 17-22. Editor(s): Brown, Fred. Cold Spring Harbor Laboratory Press: Cold Spring Harbor, N. Y.
CODEN: 64QNAJ

DOCUMENT TYPE: Conference
LANGUAGE: English

AB In the present work, we have used **retro**-inverso peptide analogs of the 141-159 peptide of VP1 protein of **foot**-and-mouth disease virus (FMDV). In preliminary expts., we had shown that the **retro**-inverso peptides cross-reacted with antisera against the L-peptides and vice versa. We have now extended this work to det. whether the antibodies produced by an all-D-**retro**-peptide will neutralize FMDV in vitro and afford protection in vivo.

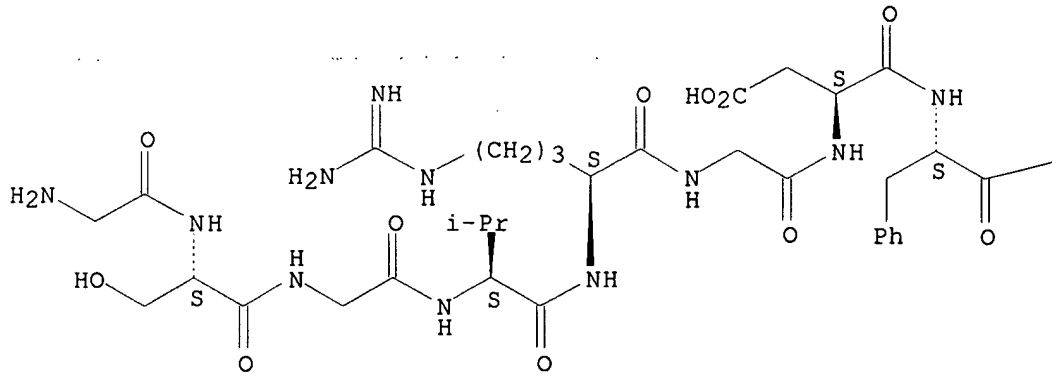
IT **164259-71-6P**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(antigenic mimicry with all-D-**retro** peptide corresponding to immunodominant loop of VP1 of **foot**-and-mouth disease virus)

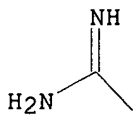
RN 164259-71-6 HCAPLUS

CN L-Leucine, glycyl-L-serylglycyl-L-valyl-L-arginylglycyl-L-.alpha.-aspartyl-L-phenylalanylglycyl-L-seryl-L-leucyl-L-alanyl-L-prolyl-L-arginyl-L-valyl-L-alanyl-L-arginyl-L-glutaminyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





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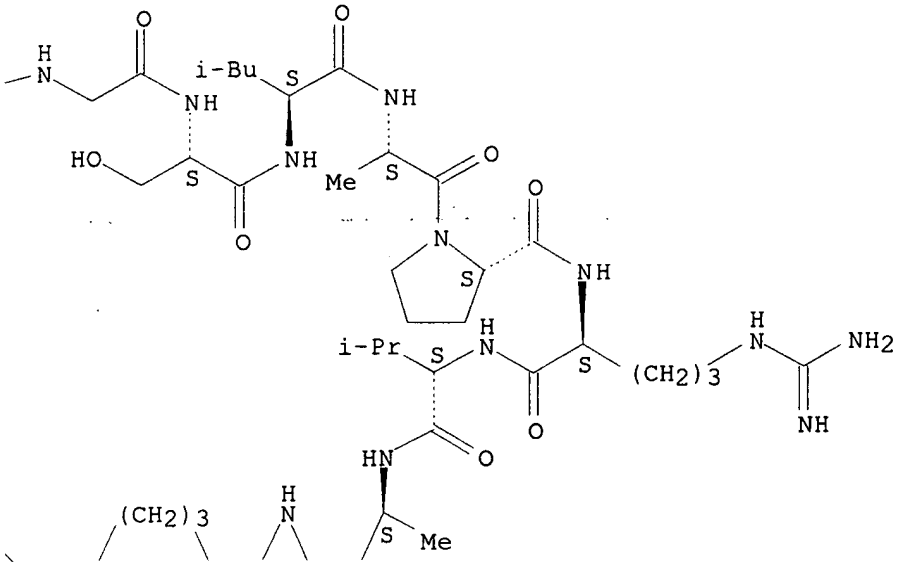

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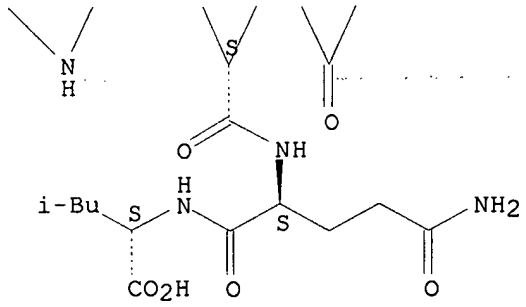


L11 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:697330 HCAPLUS
DOCUMENT NUMBER: 125:325777
TITLE: Mimicry of viral epitopes with **retro**-inverso peptides of increased stability
AUTHOR(S): Benkirane, N.; Guichard, G.; Briand, J. P.; Muller, S.; Brown, F.; Van Regenmortel, M. H. V.
CORPORATE SOURCE: Institut de Biologie Moleculaire et Cellulaire, CNRS, Strasbourg, Fr.
SOURCE: Developments in Biological Standardization (1996), 87(New Approaches to Stabilisation of Vaccines Potency), 283-291
CODEN: DVBSA3; ISSN: 0301-5149
PUBLISHER: Karger

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two major limitations to the use of peptides as synthetic vaccines are their poor immunogenicity and low antigenic cross-reactivity with the epitopes of virus particles. Recently it has been shown that **retro**-inverso peptides corresponding to an immunodominant epitope of **foot**-and-mouth disease virus (FMDV) are able to mimic the structure and antigenic activity of natural L-peptides. A series of L- and **retro**-inverso peptides of the loop 141-159 of the VP1 protein of FMDV has been synthesized. Antibodies to these peptides were produced by injecting rabbits with peptides covalently coupled to small unilamellar liposomes contg. monophosphoryl lipid A as adjuvant. The **retro**-inverso peptides led to higher serum antibody titers which appeared earlier after the start of immunization and lasted longer than those found with L-peptides. Antibodies to **retro**-inverso peptides cross-reacted strongly with L-peptides and with virus particles, while guinea pig antisera to VP1 protein and virions cross-reacted strongly with the **retro**-inverso peptides. In view of their increased stability compared to natural L-peptides, **retro** -inverso peptidomimetics have considerable potential as synthetic viral vaccines.

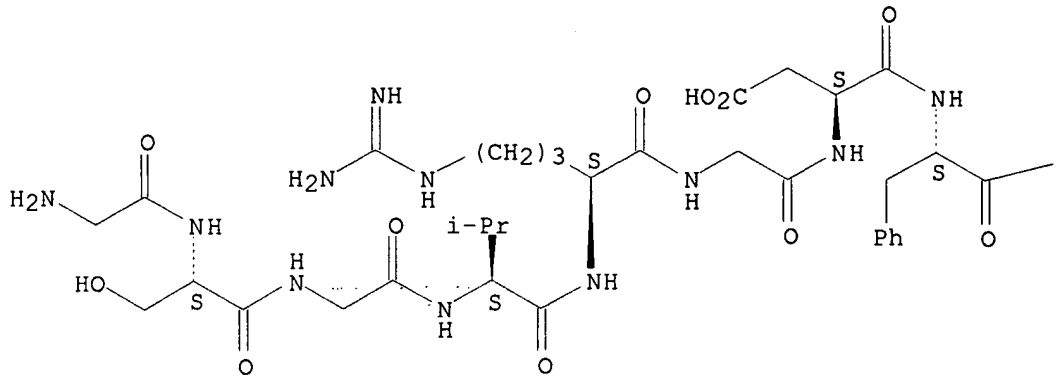
IT **164259-71-6DP**, albumin conjugates **164259-71-6P**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(mimicry of viral epitopes with **retro**-inverso peptides of increased stability)

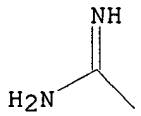
RN 164259-71-6 HCAPLUS

CN L-Leucine, glycyl-L-serylglycyl-L-valyl-L-arginylglycyl-L-.alpha.-aspartyl-L-phenylalanylglycyl-L-seryl-L-leucyl-L-alanyl-L-prolyl-L-arginyl-L-valyl-L-alanyl-L-arginyl-L-glutaminyl- (9CI) (CA INDEX NAME)

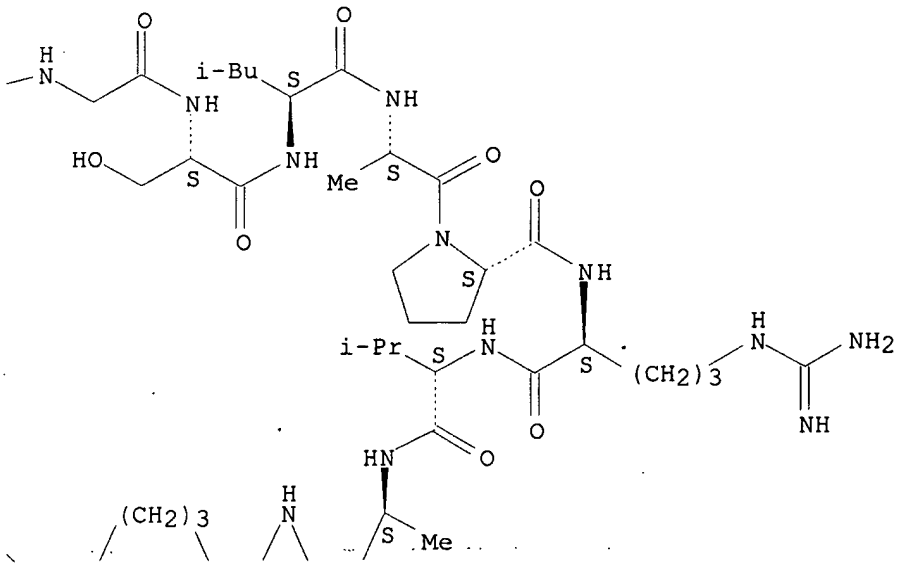
Absolute stereochemistry.

PAGE 1-A





PAGE 1-B



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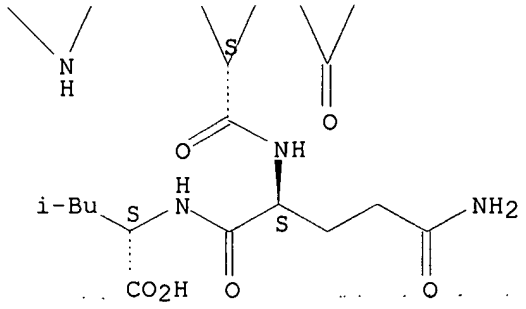
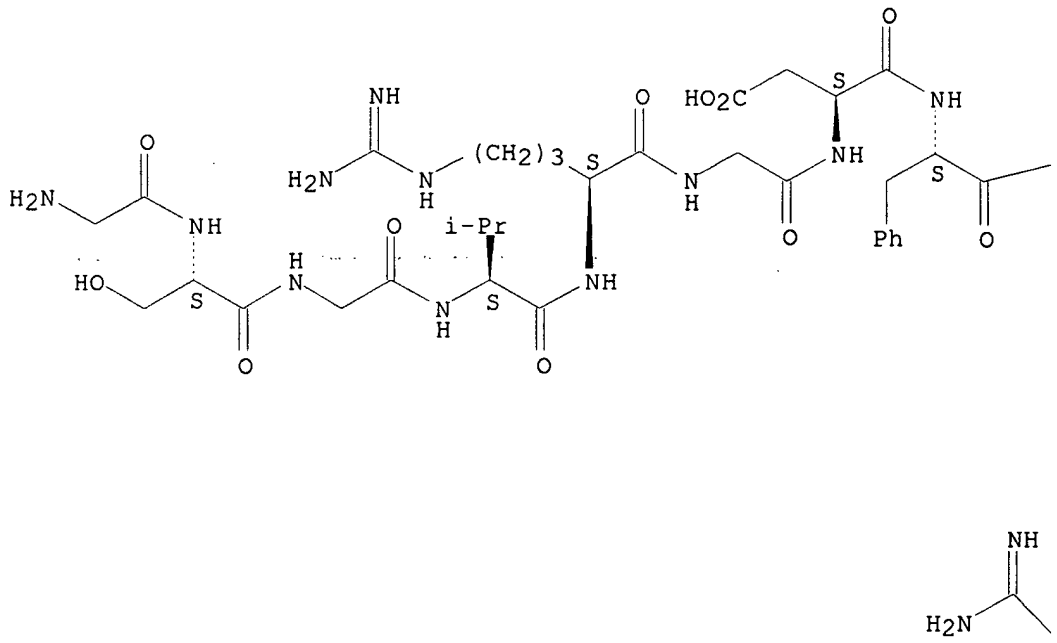


RN 164259-71-6 HCAPLUS
CN L-Leucine, glycyl-L-serylglycyl-L-valyl-L-arginylglycyl-L-.alpha.-aspartyl-L-phenylalanylglycyl-L-seryl-L-leucyl-L-alanyl-L-prolyl-L-arginyl-L-valyl-L-alanyl-L-arginyl-L-glutaminyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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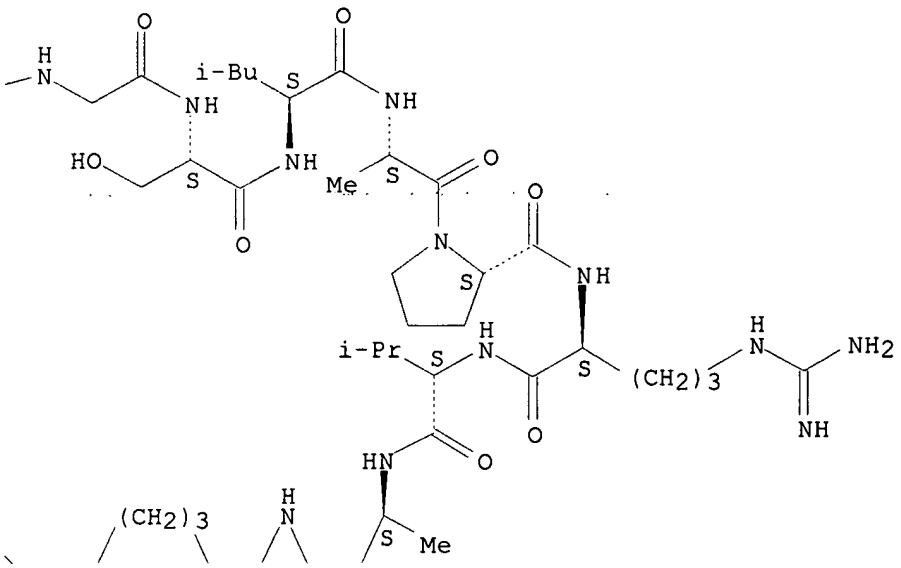
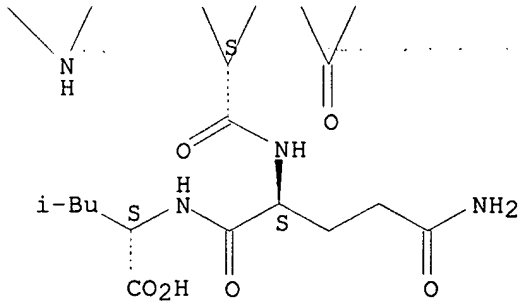


PAGE 2-B



L11 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:696116 HCAPLUS
DOCUMENT NUMBER: 126:6019
TITLE: Use of **retro**-inverso pseudopeptides for mimicking antigenic sites and as potential synthetic vaccines
AUTHOR(S): Guichard, G.
CORPORATE SOURCE: Institut de Biologie Moleculaire, Strasbourg, F-67084, Fr.
SOURCE: Peptides: Chemistry, Structure and Biology, Proceedings of the American Peptide Symposium, 14th, Columbus, Ohio, June 18-23, 1995 (1996), Meeting Date 1995, 827-828. Editor(s): Kaumaya, Pravin T. P.; Hodges, Robert S. Mayflower Scientific: Kingswinford,

UK.
CODEN: 63NTAF
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Peptides are attractive for the design of pot. synthetic vaccines. However, they are usually poorly immunogenic with limited cross-reactivity between peptide and viral epitopes. To study the usefulness of **retro**-inverso pseudopeptides as alternatives in synthetic vaccines, the author analyzed the immunodominant epitope of VP1 of **foot**-and-mouth disease virus.

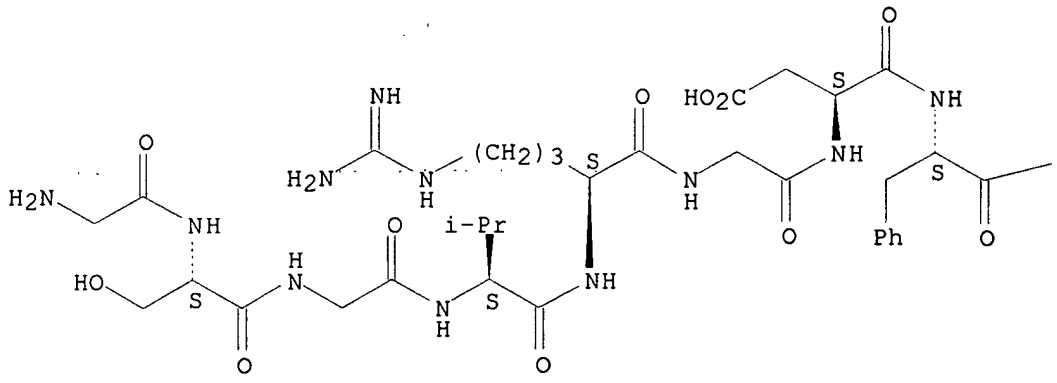
IT **164259-71-6**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(antibody binding to **retro**-inverso pseudopeptides of **foot**-and-mouth disease virus VP1 epitope)

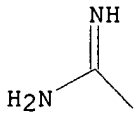
RN 164259-71-6 HCAPLUS

CN L-Leucine, glycyl-L-serylglycyl-L-valyl-L-arginylglycyl-L-.alpha.-aspartyl-L-phenylalanylglycyl-L-seryl-L-leucyl-L-alanyl-L-prolyl-L-arginyl-L-valyl-L-alanyl-L-arginyl-L-glutaminyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





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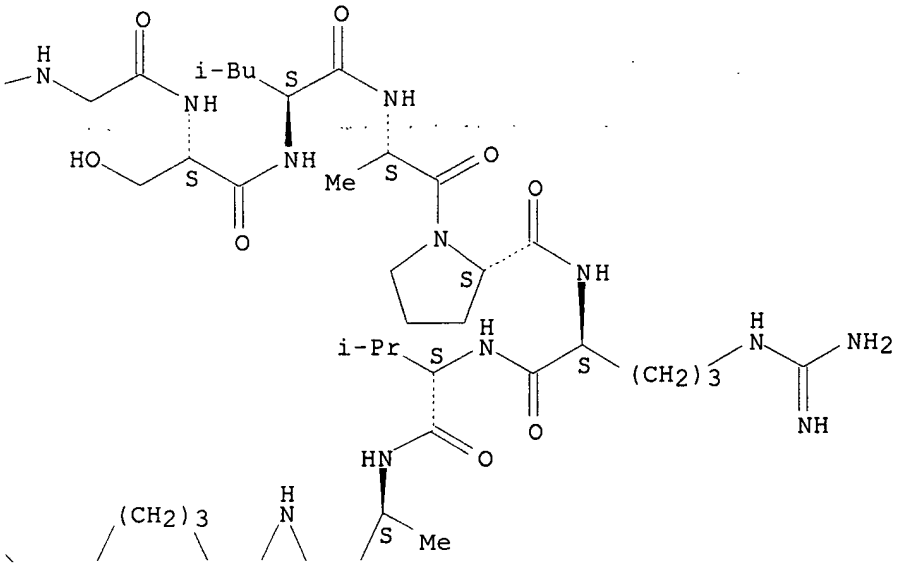

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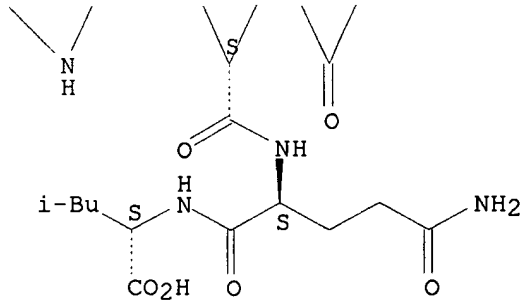


L11 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:617257 HCAPLUS
DOCUMENT NUMBER: 123:53787
TITLE: Enhanced immunogenicity and cross-reactivity of **retro**-inverso peptidomimetics of the major antigenic site of **foot**- and mouth disease virus
AUTHOR(S): Muller, S.; Guichard, G.; Benkirane, N.; Brown, F.; Van Regenmortel, M. H. V.; Briand, J. P.
CORPORATE SOURCE: Institut de Biologie Moleculaire et Cellulaire, CNRS, Strasbourg, Fr.
SOURCE: Peptide Research (1995), 8(3), 138-44
CODEN: PEREEO; ISSN: 1040-5704
PUBLISHER: Eaton

DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Retro**-inverso analogs of peptides corresponding to the major antigenic site 141-159 of VP1 from two **foot**-and-mouth disease virus variants have been synthesized and tested for their antigenic and immunogenic properties. Antibodies to the L- and **retro**-inverso peptides were produced by injecting rabbits with peptides covalently coupled to small unilamellar liposomes contg. monophosphoryl lipid A as adjuvant. When compared to the antibody response raised against the L-peptides, the duration of the IgG response that was induced by the **retro**-inverso peptides was significantly longer and the titer of anti-peptide antisera was much higher. Antibodies to **retro** -inverso peptides cross-reacted equally well with the resp. parent L-peptides. These results, obtained with a viral sequence which was found previously to represent a good candidate for possible vaccination, show that **retro**-inverse peptidomimetics could be useful for enhancing the immunogenicity of peptides.

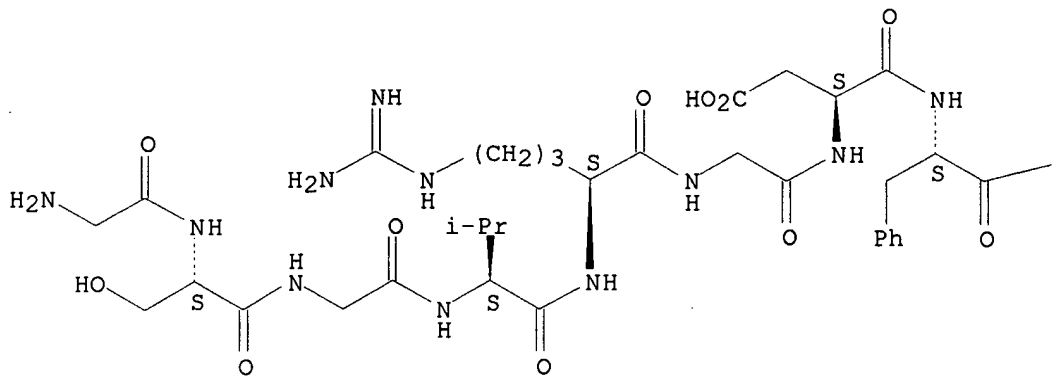
IT **164259-71-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(antigenicity and immunogenicity of **retro**-inverso peptidomimetics of **foot**-and-mouth disease virus VP1 peptides)

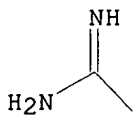
RN 164259-71-6 HCAPLUS

CN L-Leucine, glycyl-L-serylglycyl-L-valyl-L-arginylglycyl-L-.alpha.-aspartyl-L-phenylalanylglycyl-L-seryl-L-leucyl-L-alanyl-L-prolyl-L-arginyl-L-valyl-L-alanyl-L-arginyl-L-glutaminyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





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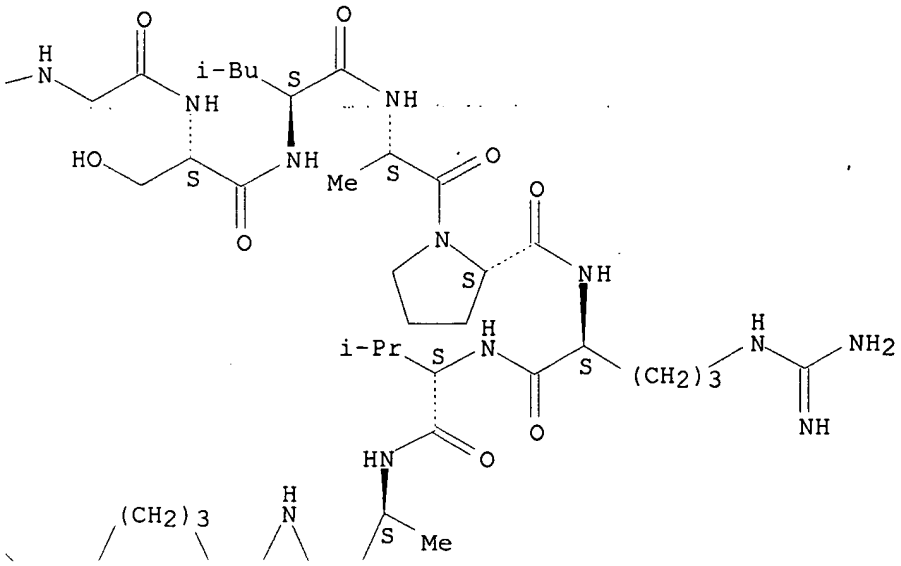

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